=> d ibib abs hitstr l13 1-27

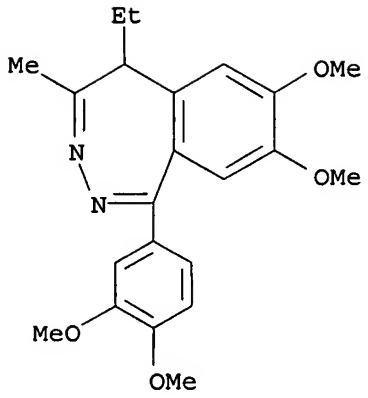
L13 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:240950 HCAPLUS
DOCUMENT NUMBER: 132:270096
TITLE: **Pharmaceutical compositions** containing an opiate analgesic and a synergizing substance
INVENTOR(S): Szekely, Jozsef; Andrasi, Ferenc; Mate, Gyorgyne; Horvath, Katalin; Horvath, Edit; Haskane, Salamon Cecilia; Aranyi, Peter; Gigler, Gabor; Fekete, Pal; Fekete, Marton
PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.; Haskane Salamon, Cecilia; et al.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020005	A1	20000413	WO 1998-HU90	19981001 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9895538	A1	20000426	AU 1998-95538	19981001 <--
PRIORITY APPLN. INFO.:			WO 1998-HU90 A	19981001 <--

AB The invention relates to a synergistic analgesic **pharmaceutical composition comprising** an opiate analgesic agent (**component** A) and a substance synergizing the analgesic effect of the opiate (**component** B) in admixt. with suitable inert solid or liquid **pharmaceutical** carriers and/or diluents. Morphine-HCl (I) (2 parts) and 5 parts by weight tofisopam (II) are dispersed in 53 parts Witepsol S 58 and melted at 50°. The still liquid suspension is filled into conical forms, solidified by cooling to 25° and the suppositories are removed from the mold. Thus suppositories having an average weight of 6 g and containing 20 mg I and 50 mg II are obtained.

IT **22345-47-7**, Tofisopam
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical compns.** containing an opiate analgesic and synergizing substance)

RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



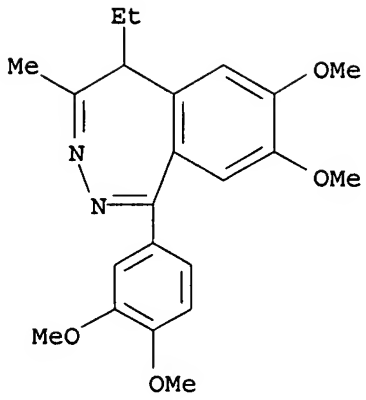
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:548268 HCAPLUS
DOCUMENT NUMBER: 131:149397
TITLE: Chemometric approach to the treatment of benzodiazepine separation and peak broadening in capillary electrophoresis
AUTHOR(S): Peyrin, Eric; Guillaume, Yves Claude
CORPORATE SOURCE: Laboratoire de Chimie Analytique, Faculte de Medecine-Pharmacie, Besancon, 25030, Fr.
SOURCE: Journal of Chromatography, A (**1999**), 849(2), 563-573
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A chemometric methodol. was used to study capillary efficiency and the separation of 10 benzodiazepines in capillary electrophoresis. The resolution between 2 adjacent peaks on the electropherogram was estimated and the overall quality of the separation was assessed by means of a new response function. The nature (methanol or acetonitrile) and proportion of the organic modifier both in the background electrolyte and the sample buffer and the injection time were considered. The results predicted that if the sample had a lower dielec. constant than the background electrolyte buffer then a much larger injection volume could be used. The **computer** optimization routine was exptl. validated and the result demonstrated that the fastest electrophoretic reparation was obtained with acetonitrile (7 min instead of 9 min with MeOH).

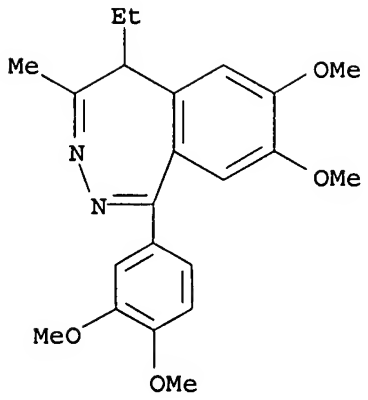
IT **22345-47-7**, Tofisopam
RL: ANT (Analyte); ANST (Analytical study)
(chemometric approach for treatment of benzodiazepine separation and peak broadening in capillary electrophoresis)

RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:529735 HCAPLUS
DOCUMENT NUMBER: 131:233625
TITLE: Novel chiroptical methods in **pharmaceutical** analysis
AUTHOR(S): Gergely, Andras; Hegedus, Hanna; Horvath, Peter; Noszal, Bela; Szasz, Gyorgy; Zsila, Ferenc
CORPORATE SOURCE: SOTE Gyogyszereszeti Kemiai Intezet, Budapest, 1092, Hung.
SOURCE: Acta Pharmaceutica Hungarica (**1999**), 69(3), 128-134
CODEN: APHGAO; ISSN: 0001-6659
PUBLISHER: Magyar Gyogyszereszeti Tarsasag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Hungarian
AB A review with 28 refs. Chiroptical spectroscopy, and its double and triple hyphenated combinations with UV-VIS spectroscopy and/or separation techniques constitute great progress in **pharmaceutical** anal., of which five recently developed methods are surveyed here, as follows: the determination of enantiomeric purity by double, CD/UV detection without, and with the latter one provides enhanced sensitivity and selectivity. The determination of chromatog. peak homogeneity, by double detection, and peak slicing by recording. The separation, identification and four stereoisomers of doubly chiral **compds.**, by HPLC separation on chiral column, and optical-chiroptical detection.
IT **22345-47-7**
RL: ANT (Analyte); ANST (Analytical study)
(novel chiroptical methods in **pharmaceutical** anal.)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:96127 HCAPLUS
DOCUMENT NUMBER: 130:144197
TITLE: Use of 2,3-benzodiazepine derivatives for the preparation of **pharmaceutical compositions** to treat diseases connected with the endogenous opioid system
INVENTOR(S): Fekete, Marton; Haller, Jozsef; Szekely, Jozsef; Horvath, Katalin; Fekete, Pal
PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9904797	A1	19990204	WO 1998-HU69		19980723	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW						
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG						
HU 9701284	A2	19990329	HU 1997-1284		19970724	<--
HU 9701284	A3	20051128				
AU 9885538	A	19990216	AU 1998-85538		19980723	<--
PRIORITY APPLN. INFO.:			HU 1997-1284	A	19970724	<--
			WO 1998-HU69	W	19980723	<--

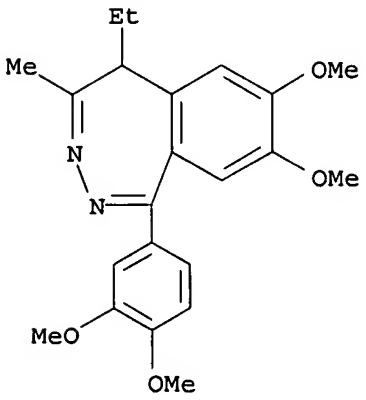
AB The invention relates to the use of 2,3-benzodiazepine derivs. for the preparation of **pharmaceutical compns.** useful for the treatment or prevention of diseases connected with the endogenous opioid system, particularly disturbances of the hedonic state. Particularly preferable 2,3-benzodiazepine derivs. for use according to the present invention are the tofisopam, girisopam, and nerisopam. The anxiolytic property of 20-80 mg/kg tofisopam was studied in rats. Granules were made from tofisopam 5, lactose 9, microcryst. cellulose 3, polyvinylpyrrolidone 0.5, and water 4 parts and dried. CM-cellulose 1.3, and magnesium

stearate 0.2 parts were added to the granules and the mixture was passed through a 1.0 mm sieve and were made up into tablets containing 50 mg tofisopam each.

IT **22345-47-7**, Tofisopam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of benzodiazepine derivs. for preparation of **pharmaceutical compns.** to treat diseases connected with endogenous opioid system)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:841273 HCAPLUS

DOCUMENT NUMBER: 124:37821

TITLE: A **comparison** of LC and SFC for cellulose- and amylose-derived chiral stationary phases

AUTHOR(S): Bargmann-Leyder, Nathalie; Tambute, Andre; Caude, Marcel

CORPORATE SOURCE: Lab. Chim. Analytique, Ecole Superieure de Physique et Chimie Industrielles de Paris, Paris, Fr.

SOURCE: Chirality (**1995**), 7(5), 311-25
CODEN: CHRLEP; ISSN: 0899-0042

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

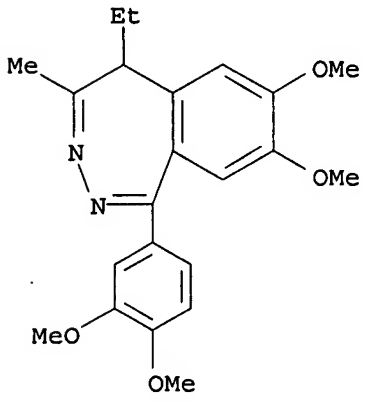
AB This study presents a systematic **comparison** of liquid chromatog. (LC) and supercrit. fluid chromatog. (SFC) for Chiralcel OD and Chiralpak AD chiral stationary phases (CSPs), performed using various chiral **compds.** having a known or potential **pharmaceutical** activity. The chiral recognition mechanisms involved in LC and SFC for the enantiomeric separation of β-blockers were studied. It appears that the presence of polar functions, like primary or secondary hydroxyl or amine functions, may result in marked discrepancies in selectivity between LC and SFC. This result is peculiar to cellulose- and amylose-derived CSPs, for which the interactions involved in chiral recognition mechanism are not always well balanced, contrary to what happens for independent CSPs. In the case of chiral resolution of polar solutes or polymer-type

CSPs, the analyst should try both the LC and SFC techniques to be able to choose the more stereoselective one.

IT **22345-47-7**, Tofisopam
RL: ANT (Analyte); ANST (Analytical study)
(liquid and supercrit. fluid chromatog. based on cellulose- and amylose-derived chiral stationary phases for drug chiral separation)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:791330 HCAPLUS

DOCUMENT NUMBER: 123:237978

TITLE: Separation of enantiomers of benzodiazepines on the Chiral-AGP column

AUTHOR(S): Fitos, I.; Visy, J.; Simonyi, M.; Hermansson, J.

CORPORATE SOURCE: Central Research Institute for Chemistry of the Hungarian Academy of Sciences, P.O. Box 17, Budapest, H-1525, Hung.

SOURCE: Journal of Chromatography, A (**1995**), 709(2), 265-73
CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

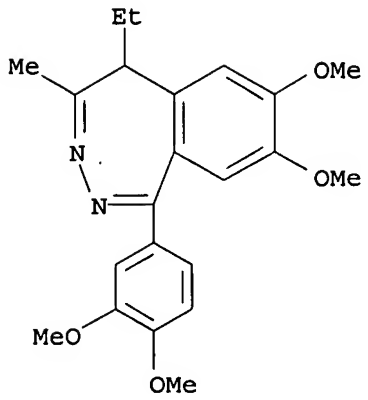
AB The resolution of twenty-five 3-chiral and 5-chiral 1,4-benzodiazepines and related **compds.** was studied on a Chiral-AGP column. Relationship between the structure and enantioselective retention is discussed stressing the role of hydrophobic and hydrogen-bonding interactions as well as the importance of the conformation of the enantiomers. The majority of the benzodiazepines were separated with high separation factors and high resolution The enantioselectivity was influenced by the nature and the concentration of the organic modifier in the mobile phase, as well as by the pH. Chiral chromatog. separation was **compared** with stereoselective binding on native AGP.

IT **22345-47-7 82059-50-5 82059-51-6**
RL: ANT (Analyte); ANST (Analytical study)
(separation of benzodiazepine enantiomers by HPLC on Chiral-AGP column)

RN 22345-47-7 HCAPLUS

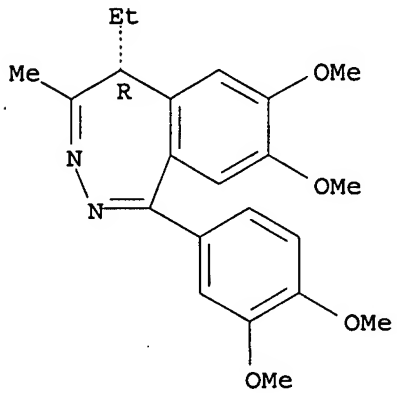
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-

methyl- (CA INDEX NAME)



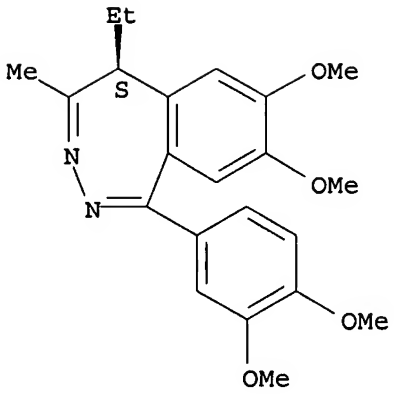
RN 82059-50-5 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 82059-51-6 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-, (5S)- (9CI) (CA INDEX NAME)

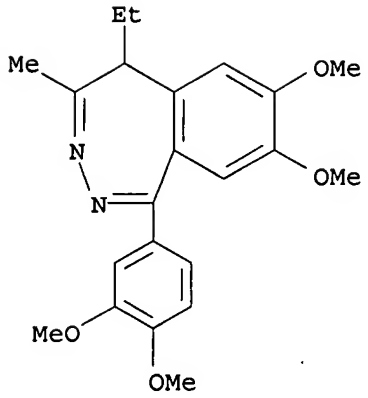
Absolute stereochemistry.



L13 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:523623 HCAPLUS
DOCUMENT NUMBER: 122:284046
TITLE: Systematic toxicological analysis using HPLC/DAD
AUTHOR(S): Tracqui, Antoine; Kintz, Pascal; Mangin, Patrice
CORPORATE SOURCE: Institut de Medecine Legale, Faculte de Medecine de Strasbourg, Strasbourg, Fr.
SOURCE: Journal of Forensic Sciences (**1995**), 40(2), 254-62
CODEN: JFSCAS; ISSN: 0022-1198
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A high-performance liquid chromatog. method with diode-array detection (HPLC/DAD) for systematic toxicol. anal. of human blood or plasma samples is presented. After single-step liquid/liquid extraction at pH 9.5 using chloroform/2-propanol/n-heptane (60:14:26, volume/volume/volume), the drugs elute isocratically from a NovaPak C18 (Waters) 4-μm Coulomb (300 mm X 3.9 mm, i.d.) at 30 degrees C, with methanol/tetrahydrofuran/pH 2.6 phosphate buffer (65:5:30, volume/volume/volume) as the mobile phase (flow rate 0.8 mL/min). Full UV spectra from 200 to 400 nm (resolution 1.3 nm) are recorded online during the 20 min chromatog. run. Solute identification may be automatically performed by **comparison** of anal. data (retention times and UV spectra) with refs. of 311 **pharmaceuticals**, toxicants and drugs of abuse stored in a **computerized** library. The method is simple, rapid, relatively inexpensive and highly specific. The previously reported applications of HPLC/DAD technol. to drug screening are reviewed, and the interests and limitations of the method are discussed in the light of this literature.

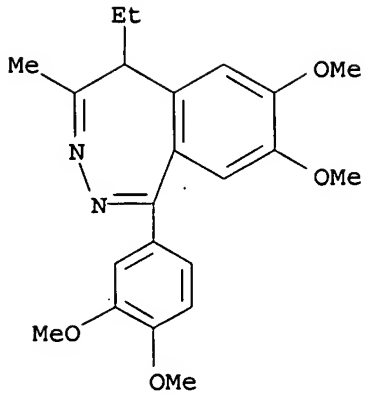
IT **22345-47-7**, Tofisopam
RL: ANT (Analyte); ANST (Analytical study)
(systematic toxicol. anal. using HPLC/DAD)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:709076 HCAPLUS
DOCUMENT NUMBER: 121:309076
TITLE: A new method of studying temperature dependence and the effect of mobile phase **composition** on the retention mechanism in reversed phase liquid chromatography
AUTHOR(S): Guillaume, Y.; Guinchard, C.
CORPORATE SOURCE: Laboratoire de Chimie Analytique, UFR des Sciences Medicales et Pharmaceutiques, Besancon, 25030, Fr.
SOURCE: Journal of Liquid Chromatography (**1994**), 17(13), 2809-20
CODEN: JLCHD8; ISSN: 0148-3919
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid procedure is used to examinate the effect of temperature and eluent **composition** on thermodn. properties in high performance liquid chromatog. is presented. The use of an exptl. design is proposed to study thermodn. solution property trends for 10 benzodiazepines. Enthalpies and entropies of transfer (mobile to stationary phase) are calculated by evaluation of Van't Hoff plots. Enthalpies of transfer are neg for all cases examined. These data show that the entropy contribution to retention becomes more significant as solvent polarity decreases. The enthalpy-entropy **compensation** behavior is tested for varying mobile phase **composition**

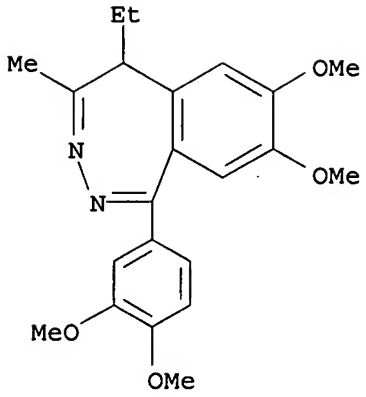
IT **22345-47-7**, Tofisopam
RL: ANT (Analyte); ANST (Analytical study)
(eluent **composition** and temperature effects on retention mechanism in reversed phase liquid chromatog. and enthalpy-entropy **compensation**)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



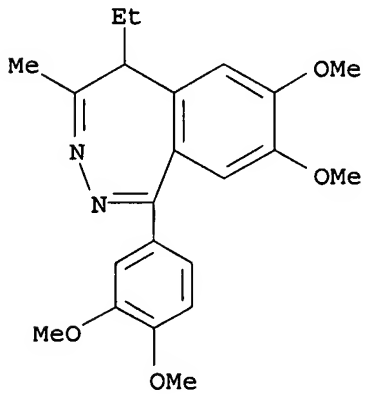
L13 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:236051 HCAPLUS
DOCUMENT NUMBER: 120:236051
TITLE: **Pharmacological** characterization of the novel anxiolytic β-carboline abecarnil in rodents and primates
AUTHOR(S): Ozawa, Masaki; Nakada, Yukie; Sugimachi, Keiko; Yabuuchi, Fumie; Akai, Tetsuo; Mizuta, Eiji; Kuno, Sadako; Yamaguchi, Motonori
CORPORATE SOURCE: Res. Dep., Nihon Schering K.K., Osaka, 532, Japan
SOURCE: Japanese Journal of Pharmacology (**1994**), 64(3), 179-87
CODEN: JJPAAZ; ISSN: 0021-5198
DOCUMENT TYPE: Journal
LANGUAGE: English

AB β-Carboline abecarnil was behaviorally and biochem. characterized as a new anxiolytic agent in rodents and primates in **comparison** with the benzodiazepine (BZ) anxiolytics. Oral treatment with abecarnil (0.5-10 mg/kg) showed a potent anticonflict activity in the water-lick test in rats. The minimal EDs was lower than those of BZ anxiolytics, such as etizolam, diazepam, clotiazepam and tofisopam. Abecarnil also showed taming effects to suppress fighting and aggressive behaviors in mice and monkeys with little sedative and ataxic effects, in contrast to the BZ anxiolytics producing marked sedative and ataxic effects. Furthermore, abecarnil suppressed both the sedative and ataxic effects induced by diazepam. Abecarnil bound to rat cerebellar BZ1 receptors (Ki = 0.24 nM) with a higher affinity than to rat spinal cord BZ2 receptors (Ki = 1.3 nM), whereas BZ derivs. bound to both the receptors with a low and equal affinity. GABA-ratios of abecarnil were 1.9 for the BZ1 receptors and 2.8 for the BZ2 receptors, and they were smaller than those of diazepam and flunitrazepam. Thus, in contrast to the BZ derivs., abecarnil may act as a selective partial agonist at central BZ1 receptors, resulting in its potent anticonflict and taming effects with little sedative and ataxic effects.

IT **22345-47-7**, Tofisopam
RL: BIOL (Biological study)
(**pharmacol.** characterization of anxiolytic abecarnil vs.)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:503037 HCAPLUS
DOCUMENT NUMBER: 119:103037
TITLE: **Pharmaceutical** technology of Grandaxin
AUTHOR(S): Fekete, Pal
CORPORATE SOURCE: EGIS Gyogyszergyar Rt., Hung.
SOURCE: Acta Pharmaceutica Hungarica (**1993**), 63(2), 67-78
CODEN: APHGAO; ISSN: 0001-6659
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Hungarian
AB A review with 6 refs. on the crystallog., particle size, solubility, moisture content stability in aqueous solution, **compressibility** and formulation of Grandaxin. Techniques for improving Grandaxin solubility are discussed.
IT **22345-47-7**, Grandaxin
RL: BIOL (Biological study)
(**pharmaceutics** of)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



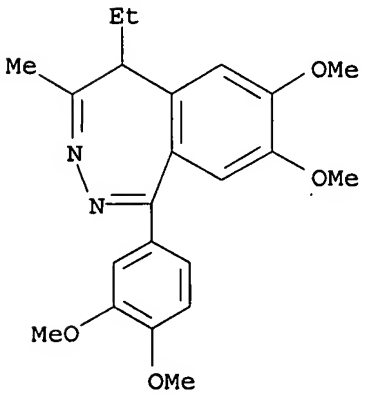
L13 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:402498 HCAPLUS
DOCUMENT NUMBER: 117:2498
TITLE: A QSAR model of teratogenesis

AUTHOR(S): Gombar, Vijay K.; Borgstedt, Harold H.; Enslein, Kurt; Hart, Jeffrey B.; Blake, Benjamin W.
CORPORATE SOURCE: Health Des., Inc., Rochester, NY, 14604, USA
SOURCE: Quantitative Structure-Activity Relationships (**1991**), 10(4), 306-32
CODEN: QSARDI; ISSN: 0931-8771
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four related QSAR models of teratogenesis in exptl. animals have been developed: one each for heteroarom., carboarom., alicyclic and acyclic **compds.** The nos. of **compds.** in these models range from 40 (for the alicyclic model) to 144 (for the carboarom. model). As determined by cross-validation using the leave-one-out, or jackknife, technique, the accuracy of the models in discriminating between teratogens and nonteratogens ranges from 92.4% to 96%. A single overall assessment of exptl. teratogenesis was chosen as the biol. endpoint; taking into account such factors as dosage, maternal toxicity, and affected organ systems remain to be subjects of further studies.

IT **22345-47-7**, Tofisopam
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(teratogenesis in laboratory animals from, QSAR model of)

RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:549643 HCAPLUS
DOCUMENT NUMBER: 115:149643
TITLE: Toxicological screening of drugs by microbore high-performance liquid chromatography with photodiode-array detection and ultraviolet spectral library searches
AUTHOR(S): Turcant, A.; Premel-Cabic, A.; Cailleux, A.; Allain, P.
CORPORATE SOURCE: Lab. Pharmacol., Cent. Hosp. Univ., Angers, 49033, Fr.
SOURCE: Clinical Chemistry (Washington, DC, United States) (**1991**), 37(7), 1210-15
CODEN: CLCHAU; ISSN: 0009-9147
DOCUMENT TYPE: Journal
LANGUAGE: English

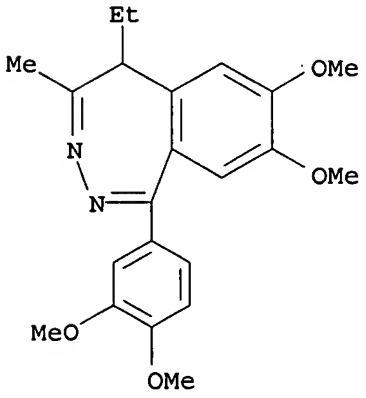
AB UV data, acquired with a photodiode-array detector coupled to a

reversed-phase liquid-chromatog. system, was used to identify unknown drugs in plasma samples of acutely poisoned patients. Both retention time and spectra of the peaks obtained with a microbore Hypersil ODS column under gradient elution are **compared** with a library of .apprx.350 **compds.** The authors three-year experience with this system, which identifies drugs in <1 h, with a high degree of confidence is presented.

IT **22345-47-7**, Tofisopam
RL: BIOL (Biological study)
(identification of, in blood of humans by microbore HPLC with photodiode-array detection, poisoning in relation to)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:618355 HCAPLUS

DOCUMENT NUMBER: 113:218355

TITLE: Retention characteristics of cyano, amino and diol precoated high-performance thin-layer chromatographic plates in the adsorption and reversed-phase separation of some benzodiazepine derivatives

AUTHOR(S): Cserhati, Tibor; Hauck, Heinz E.

CORPORATE SOURCE: Cent. Res. Inst. Chem., Hung. Acad. Sci., Budapest, H-1525, Hung.

SOURCE: Journal of Chromatography (**1990**), 514(1), 45-55
CODEN: JOCRAM; ISSN: 0021-9673

DOCUMENT TYPE: Journal

LANGUAGE: English

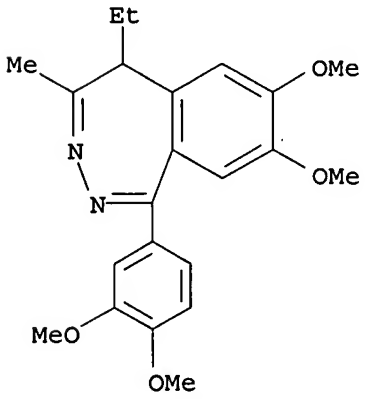
AB The retentions of 18 benzodiazepine (BZD) derivs. on CN, diol and NH2 high-performance TLC layers was determined by using 8 adsorption (CCl4-EtOAc) and 5 reversed-phase (H2O-MeOH) eluent systems. In most instances a linear correlation was found between the RM value of BZD and the EtOAc or MeOH concentration in the eluent, which allows the calcn. of the optimum eluent **composition** In aqueous eluents reversed-phase stationary phases. The differences in the reversed-phase retentions of adsorption chromatog. for their separation The low retention capacity and elongated spot shape make the NH2 plate unsuitable for the reversed-phase separation of BZD without further modification of the **composition** of the mobile phase. As chlordiazepoxide and medazepam form distorted spots on CN and diol plates, for the best separation of these BZD, NH2 plates in the adsorption separation mode

are recommended.

IT **22345-47-7**, Tofisopam
RL: ANST (Analytical study)
(retention characteristics of, on high-performance TLC, adsorption and reverse-phase separation in relation to)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:434615 HCAPLUS

DOCUMENT NUMBER: 113:34615

TITLE: **Pharmacological** validation of a novel animal model of anticipatory anxiety in mice

AUTHOR(S): Lecci, Alessandro; Borsini, Franco; Volterra, Giovanna; Meli, Alberto

CORPORATE SOURCE: Pharmacol. Res. Dep., "A. Menarini" Pharm., Florence, I-50131, Italy

SOURCE: Psychopharmacology (Berlin, Germany) (**1990**), 101(2), 255-61
CODEN: PSCHDL; ISSN: 0033-3158

DOCUMENT TYPE: Journal

LANGUAGE: English

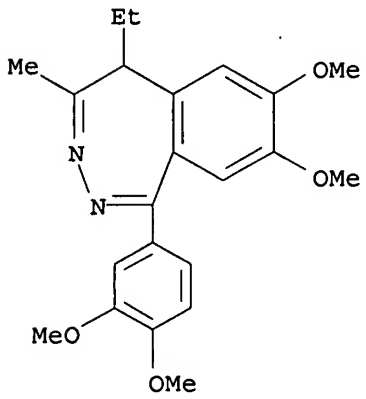
AB The current study investigates the action of anxiolytics, antidepressants, neuroleptics, antipyretics, muscle relaxants, antihypertensives and naloxone in a novel animal model of anxiety, based on the evidence that mice removed last from their cage develop hyperthermia (stress-induced hyperthermia, SIH) when **compared** to those removed first. Alprazolam (0.15-0.6 mg/kg), chlordiazepoxide (25 mg/kg), estazolam (1 mg/kg), phenobarbital (20 mg/kg), ethanol (2 and 4 g/kg), buspirone (5 and 10 mg/kg) and prazosin (1 and 2 mg/kg), as well as repeatedly administered diazepam (5 mg/kg), inhibited SIH. In contrast, tofisopam (12.5-200 mg/kg), desipramine (15 and 30 mg/kg), amitriptyline (10 mg/kg), fluoxetine (10 and 20 mg/kg), tranylcypromine (5 and 10 mg/kg), chlorpromazine (1 and 2 mg/kg), clozapine (2 and 4 mg/kg), pimozide (0.5 and 1 mg/kg), l-sulpiride (15 and 30 mg/kg), l-propranolol (5 and 10 mg/kg), acetylsalicylic acid (200 and 400 mg/kg), indomethacin (2.5 and 5 mg/kg), verapamil (2.5 and 5 mg/kg), captopril (25 and 50 mg/kg), dantrolene (10 and 20 mg/kg), mephenesin (300 and 600 mg/kg), d-amphetamine (1 and 4 mg/kg) and naloxone (2.5 and 15 mg/kg) were inactive, as were 10 mg/kg imipramine, amitriptyline and fluoxetine injected every day for 21 days. Reserpine at high doses (1.25 and 2.5

mg/kg) but not at a lower dose (0.62 mg/kg) prevented SIH, but in this case animals showed a behavioral syndrome which could have interfered with the occurrence of the hyperthermia.

IT **22345-47-7**, Tofisopam
RL: BIOL (Biological study)
(stress-induced hyperthermia response to, in anticipatory anxiety model in mice)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:175519 HCAPLUS

DOCUMENT NUMBER: 110:175519

TITLE: Removal of chromium from mother liquors in 3,4,3',4'-tetramethoxy-6-(1-acetylpropyl)benzophenone manufacture

INVENTOR(S): Lang, Ferenc; Bordas, Ferenc; Simonyi, Istvan; Kollar, Zoltan; Beniczky, Ferenc

PATENT ASSIGNEE(S): EGIS Gyogyszergyar, Hung.

SOURCE: Hung. Teljes, 12 pp.
CODEN: HUXXBU

DOCUMENT TYPE: Patent

LANGUAGE: Hungarian

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

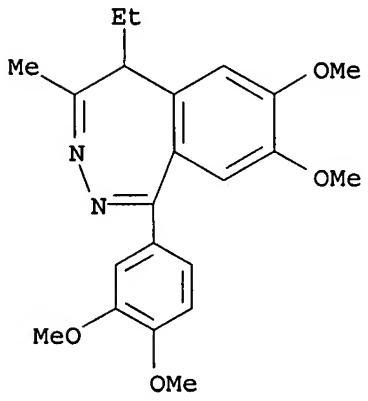
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 45474	A2	19880728	HU 1986-5511	19861230 <--
HU 202812	B	19910429		

PRIORITY APPLN. INFO.: HU 1986-5511 19861230 <--

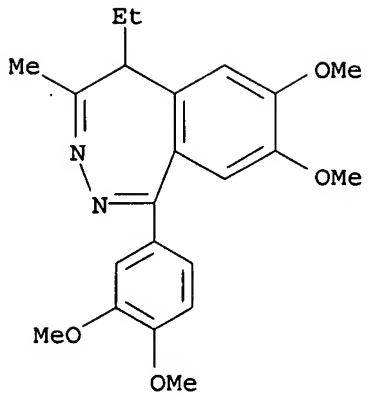
AB Cr is removed from metal liquors of the title **compound** (I) from the CrO3-catalyzed isoeugenol Me ether oxidation by treatment of the mother liquors with phosphate salts and isolation of the precipitated CrPO4. I is useful as an intermediate in the Tofisopam **pharmaceutical** manufacturing I mother liquor (50 mL) is mixed with 20 mL MeOH and 37 g Na3PO4.10H2O 2 h at 56-60°, and the precipitated CrPO4 was filtered and washed with water.

IT **22345-47-7**, Tofisopam
RL: USES (Uses)
(tetramethoxy(acetylpropyl)benzophenone intermediate for, chromium

removal from mother liquors in manufacture of)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:583451 HCAPLUS
DOCUMENT NUMBER: 109:183451
TITLE: CNS depressants accelerate the dissociation of 35S-TBPS binding and GABA enhances their displacing potencies
AUTHOR(S): Maksay, G.; Ticku, M. K.
CORPORATE SOURCE: Cent. Res. Inst. Chem., Hung. Acad. Sci., Budapest, 1525, Hung.
SOURCE: Life Sciences (**1988**), 43(16), 1331-7
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The specific binding of 35S-t-butylbicyclophosphorothionate (TBPS) was studied in synaptosomal membranes of rat cerebral cortex. The displacing potencies of 11 central nervous system (CNS) depressants and 3 convulsants were determined in the presence of 1 μM GABA and 10 nM R 5135. GABA enhanced the displacing potencies of depressants of most diverse chemical structures: diaryltriazine (LY 81067), pyrazolopyridine (etazolate), cinnamide, glutarimide, 2,3-benzodiazepine (tofizopam) alc. derivs., barbiturates, (+)-etomidate, methaqualone and meprobamate. In contrast, the displacing potencies of the convulsants [picrotoxinin, pentetrazole and the barbiturate enantiomer S(+)-MPPB] were not affected. The depressants accelerated either basal or GABA-augmented dissociation of 35-TBPS mainly by increasing the contribution of its rapid first phase. These findings suggest the contribution of a GABAergic **component** to the **pharmacol.** activity of the CNS depressants possibly by facilitating the opening of chloride channels.
IT **22345-47-7**
RL: BIOL (Biological study)
(butylbiclophosphorothionate binding to brain response to, GABAergic neurotransmission in)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)

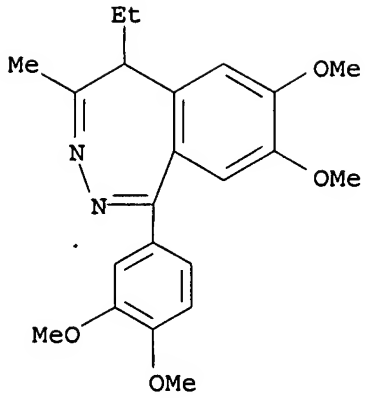


L13 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:161285 HCAPLUS
DOCUMENT NUMBER: 108:161285
TITLE: Antidepressants and metabolites that block GABAA receptors coupled to 35S-tert-butylbicyclophosphorothionate binding sites in rat brain
AUTHOR(S): Squires, Rrichard F.; Saederup, Else
CORPORATE SOURCE: Nathan Kline Inst. Psychiatr. Res., Orangeburg, NY, 10962, USA
SOURCE: Brain Research (**1988**), 441(1-2), 15-22
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Twenty-three clin. effective antidepressants and some metabolites of antidepressants (together, .apprx.50% of all antidepressants tested) fully or partially reversed the inhibitory action of 1 μM GABA on [35S]tert-butylbicyclophosphorothionate binding by rat brain. GABA antagonism, perhaps at another subset of GABAA receptors, could be also involved in clin. antidepressant action. Selective blockade by excessive GABAergic inhibition of reward systems may contribute to the clin. effects of many antidepressants, in some cases via active metabolites. Previous studies in humans on convulsant side effects of these drugs are discussed.

IT **22345-47-7**, Tofisopam
RL: BIOL (Biological study)
(GABA inhibition of butylbicyclophosphorothionate binding by brain response to, **pharmacol.** and side effects in relation to)

RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)

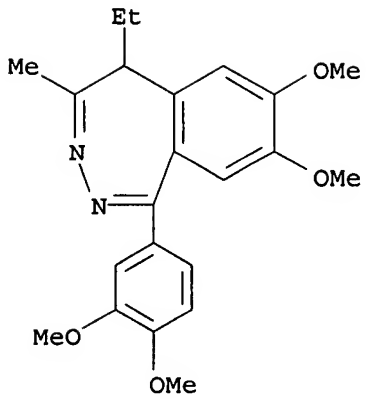


L13 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:201632 HCAPLUS
DOCUMENT NUMBER: 106:201632
TITLE: Increasing the solubility of drugs through cyclodextrin **complexation**
AUTHOR(S): Kata, M.; Selmeczi, B.
CORPORATE SOURCE: Dep. Pharm. Technol., Univ. Med. Sch., Szeged, H-6701, Hung.
SOURCE: Journal of Inclusion Phenomena (**1987**), 5(1), 39-43
CODEN: JOIPDF; ISSN: 0167-7861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclodextrin derivs. (α- [10016-20-3], β- [7585-39-9], γ- [17465-86-0] and di-Me β-cyclodextrin [51166-71-3]) increased the solubility of a number of drugs: spironolactone [52-01-7], mebendazole [31431-39-7], tofisopam [**22345-47-7**], vinpocetine [42971-09-5], metronidazole [443-48-1], furosemide [54-31-9], and hydrochlorothiazide [58-93-5]. The cyclodextrin type, combinations, ratio of drug and cyclodextrin, and other excipients all had an effect on dissoln.

IT **22345-47-7**, Tofisopam
RL: PROC (Process)
(solubilization of, by cyclodextrin **complexation**)

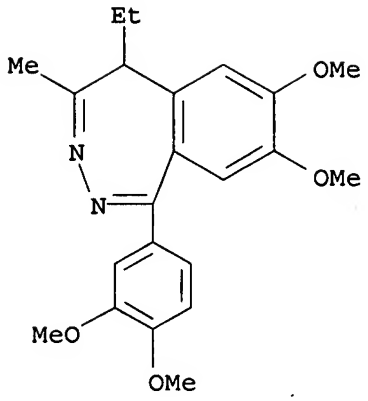
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



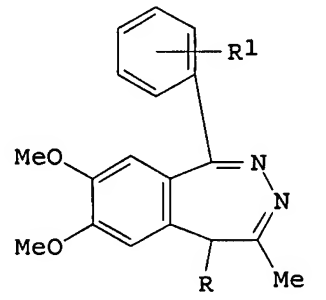
L13 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:188937 HCAPLUS
DOCUMENT NUMBER: 106:188937
TITLE: Interaction of 2,3-benzodiazepines with peripheral benzodiazepine receptors
AUTHOR(S): Kenessey, Agnes; Graf, Laszlo; Paldi-Haris, Piroska; Lang, Tibor
CORPORATE SOURCE: Inst. Drug Res., Budapest, H-1325, Hung.
SOURCE: Pharmacological Research Communications (**1987**), 19(1), 1-14
CODEN: PLRCAT; ISSN: 0031-6989
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2,3-Benzodiazepines (BZs), such as tofizopam [**22345-47-7**] and GYKI 51189 [82230-53-3] have anxiolytic potency **accompanied** by moderate sedative action, but no anticonvulsant and muscle-relaxant activities. These **compds.** show relatively low affinity to the peripheral benzodiazepine (PBZ) receptors, nevertheless, they decrease the binding of 3H-labeled RO5-4864 [14439-61-3] to its receptors in heart, kidney, and brain membranes. This diminution in the binding is due to a decrease in the affinity for the ligand without any change in the maximal number of binding sites. This interaction of 2,3-BZs with PBZ binding sites may explain their phrmacol. profile.

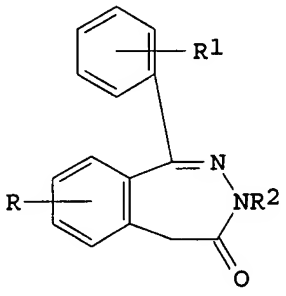
IT **22345-47-7**
RL: PROC (Process)
(binding of, to peripheral benzodiazepine receptors, **pharmacol**. in relation to)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



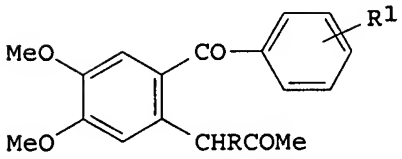
L13 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:460584 HCAPLUS
DOCUMENT NUMBER: 105:60584
TITLE: Derivatives of 2,3-benzodiazepine
AUTHOR(S): Gatta, F.; Piazza, D.; Del Giudice, M. R.; Massotti, M.
CORPORATE SOURCE: Lab. Chim. Farm., Ist. Super. Sanita, Rome, Italy
SOURCE: Farmaco, Edizione Scientifica (1985), 40(12), 942-55
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:60584
GI



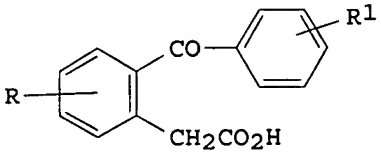
I



II



III

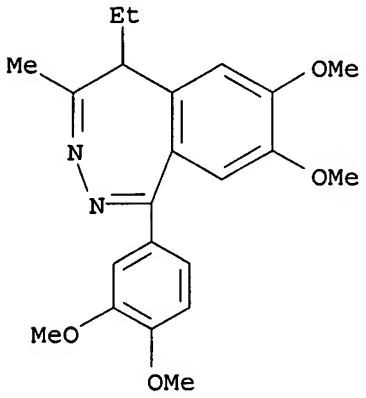


IV

AB 2,3-Benzodiazepines [I, R = H, Me or Et, R1 = H, Cl, F or 3,4-(MeO)2] or II [R = 7-MeO or 7,8-(MeO)2, R1 = H, MeO, or Cl, R2 = H or Me] were prepared by condensation of ketones (III or IV) with hydrazines. 1-Aryl-6,7-dimethoxyisochromans, obtained by condensation of 3,4-dimethoxyphenylalkanols with aromatic aldehydes, were oxidized by CrO3 to give III. Reduction of I with NaBH4 gave the corresponding 3,4-dihydro

derivs. while refluxing in Ac2O gave 3-acetyl-1-aryl-7,8-dimethoxy-4-methyl-3H-2,3-benzodiazepines. The **compds.** were evaluated with respect to their ability to bind to benzodiazepine receptors by displacement of specific 3H-diazepam binding. Only II (R = 7-MeO, R1 = 3-MeO, R2 = H) showed an affinity for the receptors similar to other know benzodiazepines. Other **compds.** exhibited lower inhibitory concns.

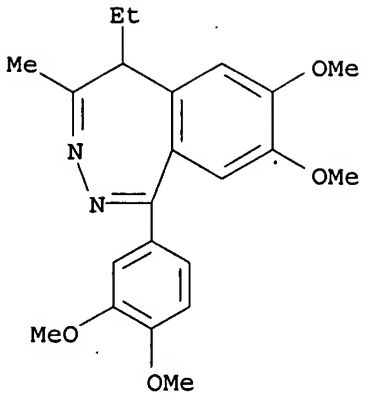
IT **22345-47-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:635502 HCAPLUS
DOCUMENT NUMBER: 101:235502
TITLE: Study of the breaking strength of ethyl cellulose microcapsules prepared by melt-dispersion method
AUTHOR(S): Devay, Attila; Racz, Istvan
CORPORATE SOURCE: Gyogyszereszeti Intez., Semmelweis Orvostud. Egy., 1092, Hung.
SOURCE: Acta Pharmaceutica Hungarica (**1984**), 54(5), 205-9
CODEN: APHGAO; ISSN: 0001-6659
DOCUMENT TYPE: Journal
LANGUAGE: Hungarian

AB The effect of the content of **components** and of the particle size on the breaking strength of tofisopam [**22345-47-7**] microcapsules, made with Et cellulose [9004-57-3] by a melt dispersion method (Devay, A., et al., 1980) was studied. A logarithmic linear relationship existed between particle size and breaking strength. An increase in the Et cellulose content enhanced the breaking strength.

IT **22345-47-7**
RL: BIOL (Biological study)
(Et cellulose microcapsules containing, breaking strength of)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:62562 HCAPLUS
DOCUMENT NUMBER: 96:62562
TITLE: Absorption, distribution, elimination and metabolism of tofizopam, a new 2,3-benzodiazepine derivative, in animal experiments
AUTHOR(S): Elekes, I.; Lang, T.; Csanyi, E.; Horvath, G.; Korosi, J.
CORPORATE SOURCE: Inst. Drug Res., Budapest, H-1325, Hung.
SOURCE: Farmaco, Edizione Pratica (**1981**), 36(12), 542-52
CODEN: FRPPAO; ISSN: 0430-0912
DOCUMENT TYPE: Journal
LANGUAGE: English
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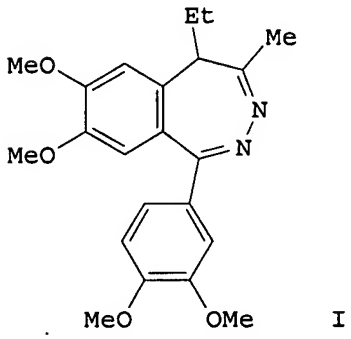


I

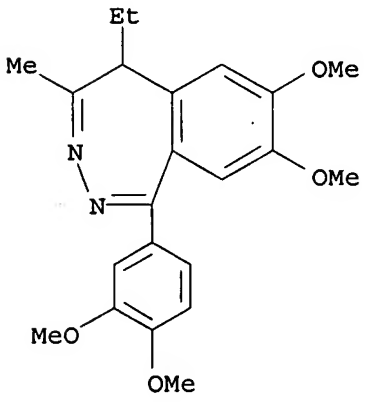
AB The **pharmacokinetic** properties and the metabolism of tofizopam (I) [**22345-47-7**] were studied in animal expts. using 14C-labeled drug. Orally administered I was absorbed rapidly by the gastrointestinal tract of rats resulting in a high and long-lasting blood level of the drug. With respect to total radioactivity, the maximum blood concentration was detected 60 min after treatment. The **compound** showed a good organ distribution and did not accumulate in any organs. Biliary excretion was very high and enterohepatic circulation was observed Radiochromatog. studies revealed the presence of the **compound** in the brain in its original form. The gastrointestinal tract absorption of I was very good in dogs;

however the maximum blood level was found 1.5 h later when **compared** to rats.

IT **22345-47-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism and **pharmacokinetics** of)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:45875 HCAPLUS

DOCUMENT NUMBER: 96:45875

TITLE: Behavioral **pharmacological** study on the structure activity relationship of benzodiazepine derivatives. With particular reference to activity of 2,3-benzodiazepine

AUTHOR(S): Ito, Chihiro

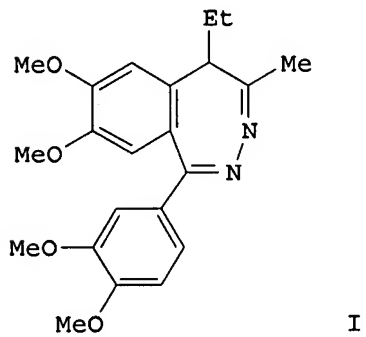
CORPORATE SOURCE: Dep. Pharmacol., Tokyo Med. Coll., Tokyo, Japan

SOURCE: Tokyo Ika Daigaku Zasshi (**1981**), 39(3), 369-84
CODEN: TIDZAH; ISSN: 0040-8905

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

GI

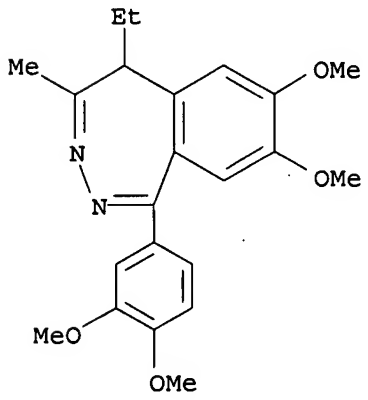


I

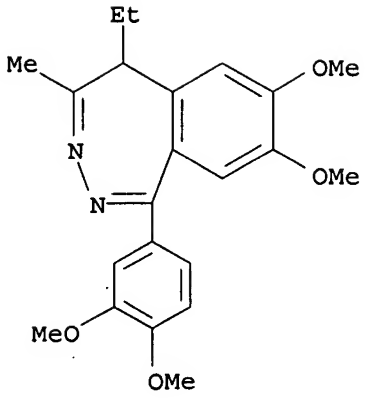
AB tofisopam (TF)(I) [22345-47-7] was similar to diazepam in its taming effects on rats and mice and in the inhibition of conflict in rats. However, its other effects such as potentiation of sleeping, reduction in motor coordination and muscle relaxation were much weaker than those of 1,4-benzodiazepines, and, therefore, these effects and the taming effects of TF were thought to be **pharmacol.** separable. TF did not show any affinity for the benzodiazepine receptor. TF had antiadrenaline, antinoradrenaline, and slight neuroleptic activities. It suppressed muricidal activity. Substituting an OH group for the methoxy group at the 7 and 8-positions of the 2,3-benzodiazepine ring and 3 and 4-position of the benzene ring of TF decreased its acute toxicity and all psychotropic activities. Antinoradrenaline activities of these related **compds** . were equivalent or less than those of TF. Apparently, the methoxy group in the chemical structure of TF is intrinsically related to its **pharmacol.** activities.

IT **22345-47-7 22345-47-7D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(behavior and central nervous system response to, mol. structure in relation to)

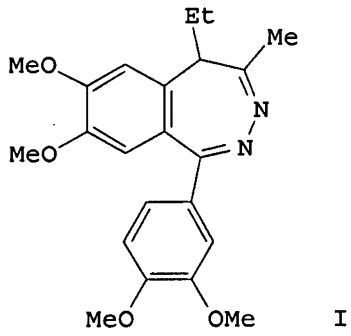
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



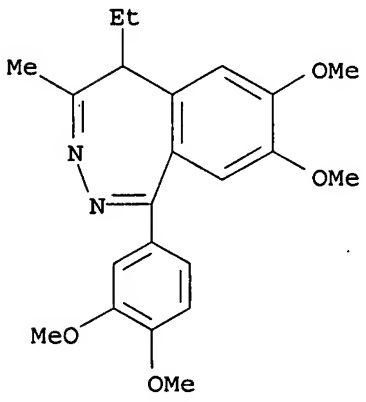
L13 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:525756 HCAPLUS
DOCUMENT NUMBER: 95:125756
TITLE: Clinical **pharmacokinetic** profile of tofisopam
AUTHOR(S): Gesztesi, A.; Sido-Lenarth, T.; Sajgo, M.; Fazekas, A.
CORPORATE SOURCE: Inst. Enzymol., Hung. Acad. Sci., Budapest, Hung.
SOURCE: Zentralblatt fuer Pharmazie, Pharmakotherapie und Laboratoriumsdiagnostik (**1981**), 120(6), 642-7
CODEN: ZPPLBF; ISSN: 0049-8696
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



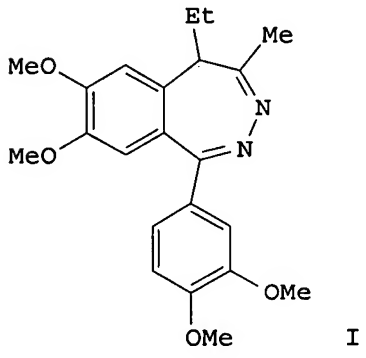
I

AB A high-pressure liquid chromatog. method is described for the determination of tofisopam (I) [**22345-47-7**] in blood serum. The mobile phase was n-heptane/isopropanol/MeOH (70:10:1) and a Lichrosorb Si-60 column was used. The separated **components** were detected at 311 nm with a limit of detection of .apprx.10 ng. The method was used to study the **pharmacokinetics** of I after different oral doses in healthy male volunteers. The absorption of I was rapid and there was a wide subject-dependent variation in the rate of I elimination. Unmetabolized I did not accumulate in blood serum even after long-term administration, suggesting that I is rapidly metabolized and eliminated in the form of metabolites.

IT **22345-47-7**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood serum by high-performance liquid chromatog., **pharmacokinetics** in relation to)
RN 22345-47-7 HCAPLUS
CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:131852 HCAPLUS
DOCUMENT NUMBER: 94:131852
TITLE: Determination of tofisopam in serum by high-performance liquid chromatography
AUTHOR(S): Sajgo, M.; Gesztesi, A.; Sido, T.
CORPORATE SOURCE: Biol. Res. Cent., Inst. Enzymol., Budapest, H-1502, Hung.
SOURCE: Journal of Chromatography (**1981**), 222(2), 303-7
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

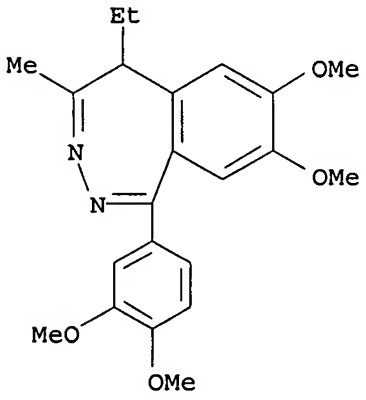
AB After the serum samples were deproteinized, they were evaporated to dryness, the residue was dissolved in 0.1M HCl, and tofisopam (I) [

22345-47-7] was extracted with CHCl3. The organic solvent was evaporated and the residue dissolved in the mobile phase, n-C7H16-iso-PrOH-MeOH (70:10:1). Chromatog. was performed on a LiChrosorb Si-60 (5 μm) column and the effluent was monitored spectrophotometrically at 311 nm. The external standard was 1-(3,4-dimethoxyphenyl)-4,5-dimethyl-7,8-dimethoxy-2,3-benzodiazepine. The I preparation used contained a 2nd **component** representing 12% of the total, thought to be a conformer of I. The calibration curve was linear in the concentration range 40-800 ng/mL. The relative standard deviation in this concentration range was 7.2%. The assay could be used to determine I **pharmacokinetics** in humans.

IT **22345-47-7**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood serum by high-performance liquid chromatog.)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:59140 HCAPLUS

DOCUMENT NUMBER: 94:59140

TITLE: Determination of eleven benzodiazepine derivatives in acetone solution by gas chromatography using a nitrogen-specific detector. **Comparison** of five stationary phases

AUTHOR(S): Barazi, Saleh; Bonini, Michelle

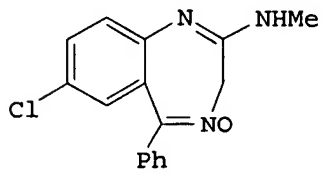
CORPORATE SOURCE: Lab. Toxicol., Univ. Bordeaux, Bordeaux, 33076, Fr.

SOURCE: Journal of Chromatography (**1980**), 202(3), 473-7
CODEN: JOCRAM; ISSN: 0021-9673

DOCUMENT TYPE: Journal

LANGUAGE: French

GI



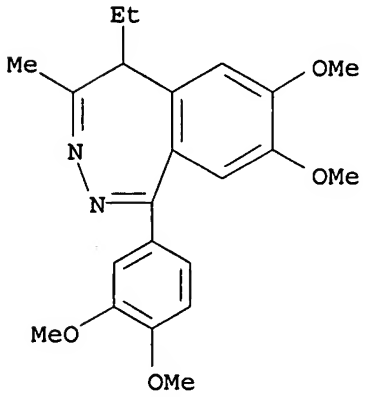
I

AB Absolute retention times and relative proportionality coeffs. are given for the gas-chromatog. separation of chlordiazepoxide (I) [58-25-3], clobazum [22316-47-8], clonazepam [1622-61-3], diazepam [439-14-5], lorazepam [846-49-1], medazepam [2898-12-6], N-demethyldiazepam [1088-11-5], mitrazepam [146-22-5], oxazepam [604-75-1], tetrazepam [10379-14-3], and tofisopam **[22345-47-7]** in pure Me2CO solns. on OV-101, -17, -25, -210, and -225 as stationary phases, using an N-P-specific thermoionic detector. Amts. from a few picograms to 1 ng could be determined, depending on the particular **compound** Only the OV-225 phase was able adequately to sep. all 11 **compds.** This system, in conjunction with the N-P-specific detector, possessed all the qualities of stability, reproducibility, sensitivity, and separatory power required for determining benzodiazepines in biol. fluids (drug overdosage, suicide, etc.) without hydrolysis or derivatization.

IT **22345-47-7**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, by gas chromatog.)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



L13 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:94763 HCAPLUS

DOCUMENT NUMBER: 88:94763

TITLE: Rapid method for the determination of the heat occurring during the **compression** of **pharmaceutical** tablets

AUTHOR(S): Kovacs, B.; Toth, Z.; Baumann-Uderszky, Judit; Gyarmati, L.

CORPORATE SOURCE: Pharm. Inst., Semmelweis Med. Univ., Budapest, Hung.

SOURCE: Pharmazeutische Industrie (**1977**), 39(10), 1010-11
CODEN: PHINAN; ISSN: 0031-711X

DOCUMENT TYPE: Journal

LANGUAGE: German

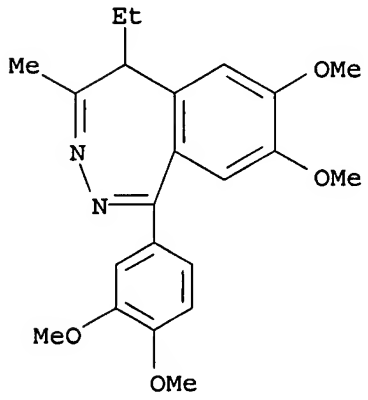
AB A method for determining the amount of heat absorbed by tablets during **compression** involves calorimetric measurement of the temperature rise of a known amount of paraffin oil into which the freshly **compressed** tablets are poured. The portable apparatus consists of measuring and reference systems, electrodes, and a digital readout device. The method can be used

with tablets of varying weight and **composition**, produced under differing pressing conditions. The mean deviation in parallel detns. on various tablets was ≤5%.

IT **22345-47-7**
RL: BIOL (Biological study)
(tablets, heat of **compression** of, determination of)

RN 22345-47-7 HCAPLUS

CN 5H-2,3-Benzodiazepine, 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl- (CA INDEX NAME)



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FILE LAST UPDATED: 5 Jul 2007 (20070705/ED)

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